REMARKS/ARGUMENTS

Claims 24, 26-28 and 40-41 are active in this application.

Claims 24 and 40 are amended to correct some typographical errors apparent from the text.

No new matter has been added.

By way of background, on pages 1-2 of the application there is a discussion that the abnormal activation of immunocompetent diseases (listing a specific set of diseases) was known. On page 2 it is described that OPN was known and used to treat autoimmune diseases such as rheumatoid arthritis. On page 3 of the application, it is stated that it was found that OPN participates in activation of immunocompetent cells and that an antibody to OPN can inhibit such activation. There are several examples in the application that show features of this statement.

On pages 2-4 of the Official Action, the Examiner has rejected all of the claims as not enabled for their full scope. In particular, on page 2, the Examiner acknowledges that the specification enables a method of treating autoimmune hepatitis with antibodies directed to a specific peptide fragment of OPN but not enablement for any and all diseases caused by the activation of immunocompentent cells using any antibody to any OPN fragment as defined in the claims.

Applicants appreciate that acknowledgement and note that (A) Claim 24, the independent claim, has been amended to define the disease as hepatitis and (B) the antibody in the claims is defined as: "which can inhibit binding between an integrin recognizing the amino acid sequence RGD (amino acids 1-3 of SEQ ID NO:1) and osteopontin or a peptide fragment thereof and wherein the antibody can inhibit binding between an integrin recognizing the amino acid sequence SVVYGLR (nucleotides 4-10 of SEQ ID NO:1) and osteopontin or a peptide fragment thereof." That is the antibody is defined by its ability to

inhibit two interactions (1) integrin that recognizes RGD (amino acids 1-3 of SEQ ID NO:1) and osteopontin (or peptide fragment) and (2) integrin that recognizes SVVYGLR (amino acids 4-10 of SEQ ID NO:1) and osteopontin (or peptide fragment).

Based on the evidence provided in the application, there should not be any question that the claims are enabled for the scope presented herein. In particular, Example 2 shows an antibody to the M5 peptide inhibited necrosis of human hepatocytes caused by hepatitis with Example 3 showing OPN expression in the liver. Example 4 also assays OPN function in hepatitis and Example 7 shows activity of the M5 antibody acting to inhibit $CD4^{+}$T cell activation. Example 8 shows neutrophil activation in relation to OPN in OPN knock-out mice and Example 10 shows a direct effect on IFN-γ.

One using polypeptides containing RGD and SVVYGLR as antigens can obtain a plurality of antibodies and then use those polypeptides for screening.

Based on this evidence, Applicants submit that it would not require undue experimentation to know and/or identify antibodies which inhibit two (2) specific interactions as defined in the claims.

Withdrawal of the rejection is requested.

The Examiner has rejected certain claims as being anticipated by the publication of WO00/63241 where Claim 24 is rejected as obvious in view of this same WO'241 further in view of a publication by Authur.

WO'241 describes modulating immune responses generally using modulators of ETA-1 also know as osteopontin. WO'241 generally describes modulating an immune response using modulators of ETA-1 which is inclusive of antibodies that block or neutralize the interaction of ETA-1 with a cell surface receptor (see page 32 of WO'241). However, while WO'241 generally describes the treatment of immune related diseases, WO'241 does not fairly suggest that hepatitis specifically could be treated with antibodies directed to the specific amino acid sequences claimed here.

Further, it is common knowledge in the field that general therapeutics for autoimmune diseases are not effective for treating hepatitis. For example, the attached four Abstracts from the PubMed database support this position:

Nat Clin Pract Gastroenterol Hepatol. 2007 Apr;4(4):202-14: Patients with HLA genotype DRB1*0301 have a poorer treatment response and a more frequent need for liver transplantation than those with HLA genotype DRB1*0401."

Dig Dis Sci. 2008 Dec 12.: "Autoimmune hepatitis (AIH) is refractory to standard therapy with prednisone and azathioprine in 20% of patients."

Am J Gastroenterol. 1999 Jan;94(1):241-8: "Autoimmune hepatitis is a form of chronic liver disease characterized by progressive hepatocellular inflammation, which usually responds to treatment with corticosteroids. However, 10% of patients with autoimmune hepatitis are refractory to corticosteroids and develop progressive liver disease and cirrhosis."

Can J Gastroenterol. 2008 Apr;22(4):388-92: "Autoimmune hepatitis (AIH) is a chronic inflammatory disease that is successfully treated with prednisone and/or azathioprine

immunosuppressive therapy in 70% to 80% of patients. The remaining patients are intolerant or refractory to these standard medications."

Further, taking the Office's own enablement rejection and applying to WO '241, yields only one conclusion--WO'241 does not enable the treatment of hepatitis. In order for a reference to anticipate a claimed invention, the reference or references must provide an enabling disclosure sufficient to place the public in possession of the claimed invention.[1] Likewise, this analysis extends to obviousness, where a holding of obviousness cannot be sustained "unless there is some known or obvious way to make the thing or to carry out the process."[2]

Reconsideration and withdrawal of both rejections citing to WO'241 is requested.

The Examiner has also rejected Claims 24-38 as being anticipated by WO02/081522. This WO'522 publication is acknowledged in the specification (see the paragraph bridging pages 2-3). As stated in the specification, WO'522 teaches the treatment of autoimmune diseases such as rheumatoid arthritis using anti OPN antibodies as the active ingredient. WO'522, however, does not teach or fairly suggest the treatment of hepatitis.

Further neither WO '241 nor WO'522 teach the relationship between the antibody defined in claim 24 and hepatitis treatment. Therefore, one would not have any incentive to combine the disclosures of these two citations for the purpose of treating hepatitis as defined in the claims.

Accordingly, withdrawal of the rejection is requested.

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[1]See MPEP 2121.01 and *In re Hoeksema*, 399 F.2d 269, 158 USPQ 596 (CCPA 1968).

[2]See *In re Collins*, 462 F.2d 538, 174 USPQ 333 (CCPA 1972), citing *In re Hoeksema*, see *supra*.

The final two rejections are provisional rejections citing two co-pending application 11/836,078 and 11/755,671 each directed to the treatment of rheumatoid arthritis. As rheumatoid arthritis is different than hepatitis (as claimed in the present application), it is believed that these rejections are no longer applicable. Withdrawal of these provisional rejections is requested.

Finally, with respect to the Examiner's comment concerning the Information Disclosure Statement, Applicants records show that all of the references were, in fact, provided to the Office on February 15, 2006. Nonetheless, the Patent Office file appears to be missing those references and therefore Applicants submit courtesy copies of those references for the Examiner's consideration.

There being no further issues, a Notice of Allowance is requested.

Respectfully submitted,

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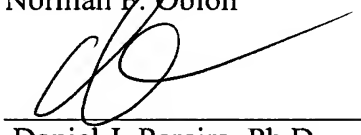

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